

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Original) A method of treating or preventing a disease selected from the group of skin diseases and diseases of the mucosa, comprising administering topically to a mammal in need of such a treatment a topical medicinal product comprising a lipopeptide or a mixture thereof, wherein said lipopeptide comprises a peptide antigen specific for a T cell population, said peptide antigen being coupled covalently with a lipid radical and being capable of activating the T cell population.

2. (Original) The method of claim 1, wherein the T cell population is a CD8+ T cell population, a CD4+ T cell population or a Tr1 cell population.

3. (Currently amended) The method of claim 1 ~~or 2~~, wherein between  $1\mu\text{g}/\text{cm}^2$  to  $500\mu\text{g}/\text{cm}^2$ , preferably  $10\mu\text{g}/\text{cm}^2$ , of said lipopeptide is administered topically to said mammal.

4. (Currently amended) The method of ~~anyone of claims 1 to 3~~ claim 1, wherein the lipid radical of the lipopeptide is derived from a fatty acid.

5. (Original) The method of claim 4, wherein the fatty acid is palmitic acid.

6. (Currently amended) The method of ~~anyone of claims 1 to 5~~ claim 1, wherein the topical medicinal product further comprises a pharmaceutically topical acceptable carrier.

7. (Currently amended) The method of ~~anyone of claim 1 to 6~~ claim 1, further comprising, prior to the topical administration of the lipopeptide, an immunisation step of the mammal with the peptide antigen or with a polypeptide comprising the peptide antigen.

8. (Original) The method of claim 7, wherein the prior immunisation is made subcutaneously or intraperitoneally.

9. (Currently amended) The method of ~~anyone of claim 1 to 6~~ claim 1, wherein the peptide antigen has been used to activate *in vitro*, as a T cell population, a Tr1 cell population obtained from a CD4+ T cell population of said mammal, and wherein said method further comprises the administration of the Tr1 cell population activated by said peptide antigen, the topical administration of the lipopeptide being made sequentially, simultaneously or separately with the administration of the Tr1 cell population.

10. (Original) The method of claim 9, wherein the peptide antigen-activated Tr1 cell population which is administered to the mammal is from  $10^6$  to  $10^9$  cells/kg.

11. (Original) The method of claim 10, wherein the peptide antigen-activated Tr1 cell population which is administered to the mammal is from  $0.5 \times 10^7$  to  $1.5 \times 10^7$  cells/kg, preferably  $10^7$  cells/kg.

12. (Currently amended) The method of ~~anyone of claims 9 to 11~~ claim 9, comprising intravenous, intramuscular, intra-arterial, intramedullary, intrathecal, intraventricular, transdermal or subcutaneous administration of the peptide antigen-activated Tr1 cell population.

13. (Currently amended) The method of ~~anyone of claims 1 to 12~~ claim 1, wherein the skin disease is selected from the group comprising psoriasis, vitiligo, prurigo, pityriasis, eruptive cutaneous mastocytosis, scleroderma, bullous dermatitis, cutaneous emphysema, erythema, eczema, acne, oedema, graft rejection and melanoma.

14. (Original) The method of claim 13, wherein the skin disease is a local inflammatory skin reaction resulting from an outside attack such as a burn, a radiation, a cut, a sting, a graft, or due to an allergen or microbe.

15. (Currently amended) The method of ~~anyone of claims 1 to 12~~ claim 1, wherein the disease of the mucosa is selected from the group comprising mucosal psoriasis, candidosis, autoimmune bullous dermatitis, erythema, syphilis, Ducrey's disease, melanoma and disorders such as viral ulcerations and bacterial infections.

16. (Currently amended) The method of ~~anyone of claims 1 to 15~~ claim 1, wherein the topical medicinal product is intended to be administered at the inflammation site.

17. (Currently amended) The method of ~~anyone of claims 2 to 6 and 9 to 16~~ claim 2, wherein the Tr1 cell population is a CD3+CD4+ CD18brightCD49b+ cell population.

18. (Currently amended) The method of ~~anyone of claims 9 to 17~~ claim 9, wherein the peptide antigen-activated Tr1 cell population is obtained by an *in vitro* preparation process comprising the following steps:

- i) obtaining a Tr1 cell population from the CD4+ T lymphocyte population of the mammal in need of the treatment;
- ii) *in vitro* activating the Tr1 cell population by contacting it with the peptide antigen; and
- iii) recovering the peptide antigen-activated Tr1 cell population.

19. (Original) The method of claim 18, wherein the step i) of obtaining the Tr1 cell population comprises the following steps:

- a) isolating a progenitor cell population from said mammal;
- b) obtaining a population of dendritic cells by culturing said progenitor cell population in presence of interleukine -10 (IL-10);
- c) contacting cells of step b) with the CD4+ T lymphocyte population isolated from said mammal to allow differentiation of said CD4+ T lymphocytes into the Tr1 cell population; and
- d) recovering the Tr1 cell population from the step c).

20. (Original) The method of claim 18, wherein the step i) of obtaining the Tr1 cell population comprises the following steps:

- a) contacting the CD4<sup>+</sup> T lymphocyte population with an appropriate amount of alpha-interferon ( $\alpha$ -IFN); and
- b) recovering the Tr1 cell population.

21. (Original) The method of claim 20, wherein the step a) of contacting is in combination with an appropriate amount of IL-10, such as 100 Uml<sup>-1</sup>.

22. (Original) The method of claim 20, wherein the Tr1 cell population is further proliferated in interleukine 15 (IL-15).

23. (Currently amended) The method of ~~anyone of claims 9 to 17~~ claim 9, wherein the peptide antigen-activated Tr1 cell population is obtained by an *in vitro* preparation process comprising the following steps:

- i) *in vitro* activating the CD4<sup>+</sup> T lymphocyte population in presence of the peptide antigen, presented by artificial antigen presenting cells; and
- ii) recovering an activated CD4<sup>+</sup> T lymphocyte population comprising at least 10% of the peptide antigen-activated Tr1 cell population.

24. (Original) The method of claim 23, wherein the artificial antigen presenting cells express a HLA II system molecule and a human LFA-3 molecule, and don't express the co-stimulation molecules B7-1, B7-2, B7-H1, CD40, CD23 and ICAM-1.

25. (Currently amended) The method of ~~anyone of claim 9 to 17~~ claim 9, wherein the peptide antigen-activated Tr1 cell population is obtained by an *in vitro* preparation process comprising the following steps:

- i) *in vitro* activating the CD4<sup>+</sup> T lymphocyte population in presence of the antigen and an appropriate amount of interleukine -10 (IL-10); and
- ii) recovering the peptide antigen-activated Tr1 cell population.

26. (Original) The method of claim 17, wherein the Tr1 cell population is purified with Elisa, flow cytometry and/or immunoaffinity using the following antibodies :

- anti-CD4, and
- anti-CD3, and
- anti-CD18, and
- anti-CD49b.

27. (Original) The method of claim 26, wherein enrichment of CD3+CD4+CD18<sup>bright</sup>CD49b<sup>+</sup> cells from a T cell population comprises the following steps :

- depletion of the total population with anti-human Ig-magnetic beads of cells bound with human anti-CD8, anti-CD14, anti-CD56 and anti-CD19, and
- selection of CD49b<sup>+</sup> cells bound to an anti-CD49b human antibody with anti-human Ig-magnetic beads.

28. (Currently amended) The method of ~~anyone of claims 1 to 27~~ claim 1, wherein the mammal in need of such a treatment is a human being.

29. (Currently amended) A pharmaceutical formulation comprising the lipopeptide of ~~anyone of claims 1 to 5~~ claim 1, together with a pharmaceutically topical acceptable carrier, wherein said lipopeptide comprises a peptide antigen specific for a T cell population, said peptide antigen being coupled covalently with a lipid radical and being capable of activating the T cell population.

30. (Original) The pharmaceutical formulation of claim 29, wherein the T cell population is a CD8<sup>+</sup> T cell population, a CD4<sup>+</sup> T cell population or a Tr1 cell population.

31. (Currently amended) The pharmaceutical formulation of claim 29 ~~or 30~~, further comprising, as a combined preparation, the peptide antigen or a polypeptide comprising the peptide antigen to be administered prior to the topical administration of the lipopeptide in an immunisation step.

32. (Original) The pharmaceutical formulation of claim 31, wherein the prior immunisation is made subcutaneously or intraperitoneally.

33. (Currently amended) The pharmaceutical composition of claim 29 ~~or 30~~, further comprising, as a T cell population, a Tr1 cell population obtained from a CD4+ T cell population of said mammal, said lipopeptide and said Tr1 cell population being administered simultaneously, separately or sequentially to said mammal.

34. (Original) The pharmaceutical composition of claim 33, wherein the peptide antigen-activated Tr1 cell population which is administered to the mammal is from  $10^6$  to  $10^9$  cells/kg.

35. (Currently amended) The pharmaceutical composition of claim 33 ~~or 34~~, wherein the peptide antigen-activated Tr1 cell population which is administered to the mammal is from  $0.5 \times 10^7$  to  $1.5 \times 10^7$  cells/kg, preferably  $10^7$  cells/kg.

36. (Currently amended) The pharmaceutical composition of ~~anyone of claims 33 to 35~~ claim 33, comprising:

- topical administration of the lipopeptide at the inflammation site, and
- intravenous, intramuscular, intra-arterial, intramedullary, intrathecal, intraventricular, transdermal or subcutaneous administration of the peptide antigen-activated Tr1 cell population.

37. (Currently amended) The pharmaceutical composition of ~~anyone of claims 29 to 36~~ claim 29, for treating or preventing a mammal suffering from a disease selected from the group of skin diseases and diseases of the mucosa.

38. (Original) The pharmaceutical composition of claim 37, wherein the skin disease is selected from the group comprising psoriasis, vitiligo, prurigo, pityriasis, eruptive

cutaneous mastocytosis, scleroderma, bullous dermatitis, cutaneous emphysema, erythema, eczema, acne, oedema, graft rejection and melanoma.

39. (Original) The pharmaceutical composition of claim 37, wherein the skin disease is a local inflammatory skin reaction resulting from an outside attack such as a burn, a radiation, a cut, a sting, a graft, or due to an allergen or microbe.

40. (Original) The pharmaceutical composition of claim 37, wherein the disease of the mucosa is selected from the group comprising mucosal psoriasis, candidosis, autoimmune bullous dermatitis, erythema, syphilis, Ducrey's disease, melanoma and disorders such as viral ulcerations and bacterial infections.

41. (Currently amended) The pharmaceutical composition of ~~anyone of claims 30 to 40~~ claim 30, wherein the Tr1 cell population is a CD3+CD4+CD18brightCD49b+ cell population.

42. (Currently amended) ~~Use of~~ A method of manufacturing a topical medicinal product for treating or preventing a disease selected from the group of skin diseases and diseases of the mucosa comprising adding a lipopeptide or a mixture thereof into the topical medicinal product, wherein said lipopeptide comprises a peptide antigen specific for a T cell population, said peptide antigen being coupled covalently with a lipid radical and being capable of activating the T cell population, ~~for the manufacture of a topical medicinal product for treating or preventing a disease selected from the group of skin diseases and diseases of the mucosa.~~

43. (Currently amended) The ~~use~~ method of claim 42, further comprising, packaging as a combined preparation, the peptide antigen or a polypeptide comprising the peptide to be administered prior to the topical medicinal product in an immunisation step.

44. (Original) A cosmetic formulation comprising a lipopeptide or a mixture thereof, wherein said lipopeptide comprises a peptide antigen specific for a T cell population, said

antigen being coupled covalently with a lipid radical and being capable of activating the T cell population, together with a cosmetically acceptable carrier, to prevent or treat disorders selected from chronic inflammatory disorders associated with ageing and its effects and autoimmune pathological disorders.



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